Applicants reserve the right to refile claims to the non-elected inventions in one or more future applications retaining the priority date of the present case and the earlier cited priority applications.

Please amend the claims so that the text of the amended claims read as follows:

1. (Amended) An isolated nucleic acid molecule comprising at least 34 contiguous nucleotides from SEQ ID NO:3.

2. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 4; and

(b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO:3or the complement thereof.

RESPONSE

I. Restriction Requirement

The Examiner has determined that the original claims are directed to three separate and distinct inventions under 35 U.S.C. § 121, as follows:

Group I: Claims 1-2, said to be drawn to an isolated nucleic acid molecule comprising at least 24 contiguous nucleotides of SEQ ID NO:3 and an isolated nucleic aid molecule that encodes the amino acid sequence of SEQ ID NO:4 and hybridizes under stringent hybridization conditions to SEQ ID NO:3, classified in class 536, subclass 23.2;

Group II: Claim 3, said to be drawn to an isolated nucleic acid molecule encoding the amino acid sequence of SEQ ID NO:6, classified in class 536, subclass 23.2; and

Group III: Claim 4, said to be drawn to an isolated nucleic acid molecule encoding the amino acid sequence of SEQ ID NO:2, classified in class 536, subclass 23.2.

In response to the Restriction Requirement, Applicants [illegible] made by Applicants' representative Lance K. [illegible]

[illegible] SEQ ID NO [illegible]

molecule that encodes the amino acid sequence of SEQ ID NO:4 and hybridizes under stringent hybridization conditions to SEQ ID NO:3, classified in class 536, subclass 23.2. Accordingly, claims 3-4 were canceled without prejudice and without disclaimer by the Examiner under 37 C.F.R. § 1.142(b) as being drawn to non-elected inventions.

Applicants reserve the right to refile claims to the non-elected inventions in one or more future applications retaining the priority date of the present case and the earlier cited priority applications.

iii. Status of the Claims

Claims 3-4, representing the Group II and III inventions, have been canceled without prejudice and without disclaimer by the Examiner under 37 C.F.R. § 1.142(b) as being drawn to a non-elected invention. No claims of the Group I invention have been canceled. Claims 1 and 2 have been amended. No new claims have been added.

Claims 1-2 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**. In compliance with 37 C.F.R. § 1.121(c)(1)(ii), a marked up copy of the original claims is attached hereto as **Exhibit B**.

IV. Support for the Claims

Claim 1 has been amended to further clarify the claim, and to recite that the isolated nucleic acid molecule comprises at least 34 contiguous nucleotides from SEQ ID NO:3. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in claim 1 as originally filed and in the specification at page 5, line 2.

Claim 2 has been amended to further clarify the claim, and to recite that the hybridization conditions are highly stringent hybridization conditions. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in claim 2 as originally filed and

V. Rejection of Claims 1 and 2 Under 35 U.S.C. § 112, First Paragraph

§§ 101 or 103, and therefore the invention has been found be have a substantial, specific, and credible utility and to be nonobvious.

The Action first rejects claims 1 and 2 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*." *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

> Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); "*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it

More recently, the standard for complying with the written description requirement of claims

> what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added)

Thus, as opposed to the situation set forth in *Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself*.

Using the nucleic acid and amino acid sequences of the present invention (as set forth in the Sequence Listing), the skilled artisan would readily be able to distinguish the claimed nucleic acids from other materials on the basis of the specific structural description provided. Polynucleotides comprising at least 34 contiguous nucleotides from the nucleotide sequence of SEQ ID NO:3, or a nucleotide sequence that encodes SEQ ID NO:4, are within the genus of the instant claims, while those that lack this structural feature lie outside the genus. Claims 1 and 2 thus meet the written description requirement.

For each of the foregoing reasons, Applicants submit that the rejection of claims 1 and 2 under 35 U.S.C. § 112, first paragraph, has been overcome, and request that the rejection be withdrawn.

Rejection of Claims 1 and 2 Under 35 U.S.C. § 112, First Paragraph

Claims 1 and 2 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject

The Action admits that the specification is enabled for "an isolated nucleic acid molecule comprising at least 24 contiguous nucleotide (*sic*) of SEQ ID NO:3 and encodes a serine protease and an isolated nucleic acid molecule encoding a protein comprising SEQ ID NO:4 and having serine protease activity" (Action at page 3). The Action then states that the specification "does not reasonably provide enablement for (1) any isolated nucleic acid molecule comprising and 24 contiguous nucleotide (*sic*) of SEQ ID NO:3 and (2) any isolated nucleic acid molecule encoding any protein comprising SEQ ID NO:4 and hybridizes under any stringent conditions to the nucleotide sequence of SEQ ID NO:3" (Action at page 3).

Applicants point out that neither of the above comments are relevant to determining whether the claimed compositions meet the legal requirements for patentability under 35 U.S.C. § 112, first paragraph. Therefore, Applicants submit that the Examiner has failed to present reasoning sufficient to establish a *prima facie* case supporting the present § 112 rejection, and accordingly the rejection is improper because: 1) the Examiner's comments were not relevant to the established legal standard of enablement; 2) the Examiner's failure to attribute adequate weight and attention to the detailed level of teaching clearly provided in the specification; and 3) the reasoning for the enablement rejection provided by the Examiner failed to adequately consider the high level of technical knowledge that can be attributed to those skilled in the art in the field of the present invention.

A. Enablement is Established by Enabling Any Practical Use

In attempting to establish a *prima facie* case to support the § 112 rejection of the composition claims, the Action questions whether the claimed compositions are sufficiently enabled to allow those skilled in the art to practice aspects of the invention involving standard molecular biological techniques. The § 112 rejection, as applied against the nucleic acid compositions, is completely misplaced. It has long been established that composition claims are enabled by defining any practical use of the claimed compound. *In re Nelson*, 126 USPQ 242 (CCPA 1960); *Cross v. Iizuka*, 224 USPQ 739 (Fed. Cir. 1985); "[U]

[illegible], 20 USPQ2d 1300, 1304 (Fed. Cir. 1991).

molecule encoding a protein comprising SEQ ID NO:4 and having serine protease activity" are enabled (Action at page 3). Thus, the enablement issue should be resolved. Enablement only requires that the specification describe a practical use for the composition defined in the claims, and that a skilled artisan be able to make and use the claimed DNA segments without undue experimentation. Accordingly, by the Examiner's own admission, the § 112 requirement has certainly been met.

The Action seems to contend that the specification provides insufficient guidance regarding the biological function or activity of certain of the claimed compositions. However, such an enablement standard conflicts with established patent law. In *In re Brana*, (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the [illegible]

Brana at 1442-1443, citations omitted. In assessing the question of whether undue experimentation [illegible]

[illegible]

not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The Examiner cites *Wands* for the proposition that the present invention could not be practiced without "undue experimentation". However, it is important to remember that, as discussed above, in assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin, supra*. In *Wands*, the P.T.O. took the position that the applicant failed to demonstrate that the disclosed biological processes of immunization and antibody selection could reproducibly result in a useful biological product (antibodies from hybridomas) within the scope of the claims. In its decision overturning the P.T.O.'s rejection, the Federal Circuit found that Wands' demonstration of success in four out of nine cell lines screened was sufficient to support a conclusion of enablement. The court emphasized that the need for some experimentation requiring, *e.g.*, production of the biological material followed by routine screening, was not a basis for a finding of non-enablement, stating:

> Disclosure in application for the immunoassay method patent does not fail to meet enablement requirement of 35 USC 112 by requiring 'undue experimentation,' even though production of monoclonal antibodies necessary to practice invention first requires production and screening of numerous antibody producing cells or 'hybridomas,' since practitioners of art are prepared to screen negative hybridomas in order to find those that produce desired antibodies, since in monoclonal antibody art one 'experiment' is not simply screening of one hybridoma but rather is entire attempt to make desired antibody, and since record indicates that amount of effort needed to obtain desired antibodies is not excessive, in view of Applicants' success in each attempt to produce antibody that satisfied all claim limitations.

Wands, at 1400. [illegible]

supra; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, *supra*

[illegible]

assessment of the ability of the skilled artisan to perform large scale screening techniques. Applicants submit that screening vast numbers of nucleic acid molecules has in fact become very routine in the art, so routine, in fact, that the Office has set forth new policies for handling the overwhelming quantity of patent applications containing large numbers of nucleic acid sequences. As these sequences are commonly generated by large scale screening efforts, Applicants are indeed hard-pressed to understand how "routine experimentation in the art does not include screening for a vast number of nucleic acid molecules". Therefore, a sufficient *prima facie* case of deficient teaching has not been established, and it is thus improper for the Examiner to require Applicants to provide rebuttal evidence since, absent the establishment of a *bona fide prima facie* case that the specification is not enabled, the legal burden remains with the Examiner.

Applicants additionally point out that significant commercial exploitation of nucleic acid sequences requires no more information than the nucleic acid sequence itself. Applications ranging from diagnostics (utilizing, for example, short oligonucleotide probes or PCR primers), gene expression analysis or profiling (utilizing, for example, arrays of short, overlapping or non-overlapping, oligonucleotides), and even gene therapy (utilizing, for example, short oligonucleotide antisense primers) are practiced utilizing nucleic acid sequences and techniques that are well-known to those of skill in the art. The widespread commercial exploitation of nucleic acid sequence information points to the level of skill in the art, and the enablement provided by disclosures such as the present specification, which include specific nucleic acid sequences and guidance regarding the various uses of such sequences.

Even though the burden has been improperly shifted to Applicants, the following section is being provided to demonstrate that the specification is fully enabling in view of the detailed guidance and teaching provided in the specification within the context of the high level of technical knowledge present in the art regarding the use of nucleic acids such as those presently claimed..

[illegible] present invention. However, as discussed above, this requirement is completely misplaced. There is

[illegible]

details in a patent specification. For example, it is not unreasonable to expect a Ph.D. level molecular biologist to be able to use the disclosed sequence to design oligonucleotide probes and primers and use them in, for example, PCR based screening and detection methods to obtain the described sequences and/or determine tissue expression patterns. Nevertheless, the present specification provides highly detailed descriptions of techniques that can be used to accomplish many different aspects of the claimed invention, including recombinant expression, site-specific mutagenesis, *in situ* hybridization, and large scale nucleic acid screening techniques, and properly incorporates by reference a montage of standard texts into the specification, such as Sambrook *et al.* (*Molecular Cloning, A Laboratory Manual*) and Ausubel *et al.* (*Current Protocols in Molecular Biology*) to provide even further guidance to the skilled artisan. Incorporation of material into the specification by reference is proper. *Ex parte Schwarze*, 151 USPQ 426 (PTO Bd. App. 1966). The § 112, first paragraph rejection is thus *prima facie* improper:

> As a matter of patent office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi & Horton, 169 USPQ 367, 369 (C.C.P.A. 1971), emphasis as in original. In any event, an alleged lack of express teaching is insufficient to support a first paragraph rejection where one of skill in the art would know how to perform techniques required to perform at least one aspect of the invention. As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands, supra.* In fact, it is preferable that what is well known in the art be omitted from the disclosure. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). As standard molecular biological techniques are routine in the art, such protocols do not need to described in detail in the specification.

Applicants submit that the specification as filed is enabled as they are supported by a specification that provides sufficient description to enable the skilled person to make and use the invention as claimed.

C. Claims 1 and 2 are Enabled

As detailed in the sections above, all aspects of the enablement rejection under 35 U.S.C. § 112, first paragraph have been overcome. Applicants therefore respectfully request that the rejection be withdrawn.

VII. Rejection of Claims 1-2 Under 35 U.S.C. § 112, Second Paragraph

The Action next rejects claims 1-2 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

The Action first rejects claims 1 as allegedly indefinite based on the term "24 contiguous bases". While Applicants submit that the term does not render the claim indefinite, the term "bases" has been replaced with the term "nucleotides". Applicants state for the record that this amendment is made solely in order to progress the case more rapidly to allowance. Applicants therefore request withdrawal of this rejection.

The Action next rejects claims 1 as allegedly indefinite based on the term "NHP". While Applicants submit that the term does not render the claim indefinite, the term "NHP" has been removed from the claim. Applicants state for the record that this amendment is made solely in order to progress the case more rapidly to allowance. Applicants therefore request withdrawal of this rejection.

The Action next rejects claim 2 as allegedly indefinite based on the term "stringent hybridization conditions", because "the specific hybridization and washing conditions are not recited in the claim" (Action at page 5). Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). However, while Applicants submit that the term is sufficiently definite, as a number of stringent hybridization conditions are defined in the specification and would be known to those of skill in the art, solely in order to progress the case more rapidly toward allowance the claim has been revised to

revised Claim 2 even more clearly meets the requirements of 35 U.S.C. § 112, second paragraph.

VIII. Rejection of Claim 1 Under 35 U.S.C. § 102(b)

The Action next rejects claim 1 under 35 U.S.C. § 102(b), as allegedly anticipated by Tsuruoka *et al.* (Accession #E13202, Alignment No. 1; "Tsuruoka"). While Applicants do not necessarily agree with the present rejection, as claim 1 has been amended to comprise at least 34 contiguous nucleotides from SEQ ID NO:3, which the Examiner agrees is not taught by Tsuruoka (Action at page 5), Applicants submit that the rejection of claim 1 under 35 U.S.C. § 102(b) has been overcome, and respectfully request withdrawal of the rejection.

IX. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Fronda have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

February 7, 2002
Date

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